REMARKS

The Final Office Action mailed June 3, 2003 has been received and reviewed. Claims 1, 4, 7-8, 13-14, 16, 18, 19, and 21-24 are currently pending. Claims 1, 4, 7-8, 13-14, 16, 18, 19 and 21-24 were rejected. Claims 1, 4, 7, 8, 16 and 21-22 have been amended. All claim amendments and cancellations are made without prejudice or disclaimer. Reconsideration of the application is respectfully requested.

Interview

Applicants would like to thank Examiners Marvich and Guzo for the courtesy extended during the interview held on August 7, 2003. Applicants found the interview to be very helpful, as evidenced by the remarks in the Interview Summary: "RCE will be filed, method claims to be pursued." Consistent with the Office's suggestion, applicants have filed a divisional application directed to methods of using the adenoviral vectors claimed in the present application.

Priority Claim

During the interview of August 7, 2003, it was noted that the priority claim of the present application to European patent application EP 98202297.2, filed July 8, 1998, which has the earliest filing date to which the present application is entitled, had not been perfected. In reply, applicants submit a supplemental declaration correctly asserting the priority claim in Appendix A. This submission clarifies that the present application is entitled to the benefit of the filing date of European patent application EP 98202297.2.

Objection to Claim 16

Claim 16 was objected to because it contained a misspelling of the term "adenovirus." The present amendment corrects this typographical error and, it is respectfully submitted, overcomes the objection. Accordingly, withdrawal of the objection is respectfully solicited.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 16 and 22 were rejected under the second paragraph of 35 U.S.C. § 112 as being assertedly indefinite. Specifically, the Office pointed out that claim 16 recited a fiber protein that "is adenovirus 35" and that a "fiber protein cannot be an adenovirus." Claim 16 has been amended to recite a fiber protein that "is from" a particular adenoviral serotype, consistent with the Office's helpful suggestion. Similar amendments were made to claims 4, 7, 8, 21, and 22 to clarify the same matter. In addition, claim 22 was amended to recite the "recombinant chimeric adenoviral vector of claim 1," which has proper antecedent basis. Accordingly, applicants respectfully request withdrawal of the rejections of claims 16 and 22 under the second paragraph of 35 U.S.C. § 112.

Claims 1, 4, 7, 8, 13, 14 and 16 were rejected under the second paragraph of 35 U.S.C. § 112 as being assertedly indefinite. Specifically, the Office pointed out that these claims recited "a first capsid" and "a second capsid" and that "it is unclear how a vector can have two" capsids. It is first noted that none of claims 13, 14, and 16 recites "a first capsid" and "a second capsid", so the rejection should not apply to those claims. Claim 1, from which claims 4, 7, and 8 depend, has been amended to recite "a first adenovirus" with "a non-native fiber protein substituted for a fiber of the first adenovirus". It is respectfully submitted the present amendment renders claims 1, 4, 7, and 8 compliant with the second paragraph of 35 U.S.C. § 112 and, thus, overcomes the rejection. Accordingly, applicants respectfully request withdrawal of the rejection of claims 1, 4, 7, 8, 13, 14 and 16.

Rejection under 35 U.S.C. § 112, First Paragraph

Claim 16 was rejected under the first paragraph of 35 U.S.C. § 112 for assertedly lacking enablement. Specifically, the Office pointed out that claim 16 recited an adenoviral nucleic acid modified such that an immune response in a host system to proteins encoded thereby is "disabled," which, the Office asserted, would require undue experimentation. Claim 16 has

been amended to delete "or disabled", which, it is respectfully submitted, overcomes the rejection. Withdrawal of the rejection is therefore respectfully solicited.

Rejections under 35 U.S.C. § 102

Claims 1, 4, 7, 8, 13, 14, 16, 18, 19, 21-24 were rejected under 35 U.S.C. § 102(e) as being assertedly anticipated by Crystal, *et al.* (U.S. Patent 6,127,525, hereinafter "Crystal"). The rejection is respectfully traversed.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. (*Verdegaal Brothers v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). The identical invention must be shown in as complete detail as is contained in the claim. (*Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989)). And the elements of the prior art reference must be arranged as required by the subject claim. (*In re Bond*, 910 F.2d 831 (Fed. Cir. 1990). *See generally* MPEP § 2131).

Crystal does not describe each and every element of the claimed invention. The Office acknowledged as much in the Office Action mailed December 17, 2002, where it stated "[t]he prior art appears to be silent with regard to chimeric viral capsids comprising protein fragments that are intended to direct the recombinant capsid to dendritic cells." (Office Action mailed December 17, 2002, p. 5, second paragraph). The fact is, Crystal is silent with respect to modifications directed to providing tropism to desired target cells and makes no mention whatsoever of dendritic cells. With such gaping omissions, Crystal simply cannot be said to anticipate claims 1, 4, 7, 8, 13, 14, 16, 18, 19, and 21-24, each of which claims an adenoviral vector modified to include a tropism for dendritic cells.

Since the express teachings of Crystal fail to describe each and every limitation of the rejected claims, the Office relies on a theory of inherency. Though it is not entirely clear, the Office appears to assert that Crystal inherently describes all chimeric adenoviral vectors with switched fiber proteins. Such an overly broad reading of Crystal is categorically disputed.

"In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *See*, M.P.E.P. § 2112, citing *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990), emphasis in original. In support of its theory of inherency, the Office asserts that "inherency is not established by probabilities or possibilities but by the property of the chimeric adenovirus as taught by applicant's own specification." Even if it were true that all adenoviral fibers have at least some tropism for dendritic cells, applicants' work demonstrated the variegation among adenoviral fibers and illuminated the specific fibers with the most advantageous tropism. Each of the pending claims is drawn to a selected specific adenovirus serotype or a group of adenovirus serotypes, which applicants' work has shown to have particularly advantageous tropism for dendritic cells.

The Office instead asserts that "applicants have not shown why one would expect that a chimeric adenovirus comprising the fiber of Ad11, Ad16, Ad35, Ad40L or Ad51 made according to the teachings of Crystal et al would not possess the ability to bind and infect dendritic cells." On the contrary, applicants' data in Examples II through IV show that not all adenoviruses have a tropism for dendritic cells and that there is much variation between serotypes for dendritic cell tropism. (*See*, Specification, p. 13, line 11 – p. 14, line 18). Indeed, the present invention is based, at least in part, on the discovery that while adenovirus serotype 5 poorly infects immature dendritic cells, chimeric adenoviruses based on serotype 5 with a fiber of another serotype show efficient infection of immature dendritic cells. (Specification, Example II, p. 13, lines 12-22). The experimental results disclosed in the present application unequivocally show the unpredictability of the art of selecting adenoviral fibers for tropism for dendritic cells and that each serotype's tropism is not predictable by simple extrapolation from other serotypes. In other words, applicants discovered for the first time which adenoviral fiber proteins have the most advantageous tropism for dendritic cells. Assuming for the sake of argument the Office is correct in asserting that all adenoviral fibers have at least some tropism for dendritic cells, Crystal cannot

be said to teach anything with respect to relative tropism among adenoviral serotypes and consequently cannot be said to teach which serotypes are most advantageous for use with dendritic cells.

As can be seen from the foregoing, Crystal neither expressly nor inherently describes adenoviruses with tropism for dendritic cells. Consequently, Crystal does not anticipate claims 1, 4, 7, 8, 13, 14, 16, 18, 19, 21-24, and withdrawal of the rejection is respectfully solicited.

ENTRY OF AMENDMENTS

Entry of the foregoing amendments is respectfully requested, as the amendments at least comply with the Office's requirements as to form (*i.e.*, claim 16). Further, it is believed the amendments overcome the rejections under 35 U.S.C. §§ 102 and 112 asserted in the Office Action. The amendments neither introduce new matter nor require further search. Should the Office disagree that the claims, as amended, define allowable subject matter, entry of the amendments is nevertheless respectfully solicited inasmuch as they place the claims in better condition for consideration on appeal.

CONCLUSION

It is believed the amendments place the claims in condition for allowance, and timely issuance of a Notice of Allowance is therefore respectfully requested. Should the Office determine that additional issues remain which might be resolved by a telephone conference, it is respectfully invited to contact applicants' attorney at the address or telephone number given herein.

Respectfully submitted,

Shawn G. Hansen
Registration No. 42,627
Attorney for Applicants
TRASKBRITT, P.C.
P.O. Box 2550
Salt Lake City, Utah 84110-2550
Telephone: 801-532-1922

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SGH/tjs

Enclosure: **Appendix A** – Supplemental Declaration

Document in ProLaw